

## **REMARKS**

### **I. Overview**

Claims 1, 4-8, 10-12 and 14-19 are pending in the present application. Claims 2-3, 9, 13 and 20-22 are cancelled.

This supplemental amendment is responding to the Notice of Non-Compliant Amendment (37 CFR 1.121) mailed April 30, 2008. The Notice indicated that claims 20-22 had not been included in the claim set. Applicant filed an Amendment After Final on September 29, 2003 cancelling claims 20-22 as drawn to a non-elected invention, however this was not shown in the claim set, which omitted claims 20-22. This omission was also present in the amendment filed November 2, 2007, which precipitated the Notice of Non-Compliant Amendment.

Herewith Applicant submits a substitute amendment which includes a complete claim set properly showing claims 20-22 as cancelled. This amendment replaces the earlier submitted amendment.

Applicants note that Appeal Brief filed on September 25, 2006 has resulted in the withdrawal of rejections to claims 1, 4-8, 10-11, 14-15 and 17-19 under 35 U.S.C. § 103(a) by De Vuyst et al. (Microbiology, Vol. 142, 1996, pages 817-827), claims 1, 4-8, 10-15 and 17-19 under 35 U.S.C. § 103(a) by De Vuyst et al., cited above, in view of Nanji (U.S. Patent 5,413,785), and claim 16 under 35 U.S.C. § 103(a) by De Vuyst et al., cited above, in view of Perdigon et al. (J. of Food Protection, Vol. 53, No. 5, pages 404-410, 1996).

Applicant has reviewed and considered the Office Action mailed July 6, 2007. Claim 1 has been amended to recite "exposing said bacteria to biological, chemical or physical stress for at least one or more sequential periods of stress". Support for the amendment may be found throughout the specification, for example, in originally filed claim 1. Claims 6 and 7 have been

amended to overcome objection formalities. No new matter has been added. Claims 1, 4-8 and 10-12 and 14-19 are pending in the instant application. In light of the remarks that follow, Applicants respectfully request reconsideration and withdrawal of the rejections.

## **II. New Claim Objections**

The Examiner states claims 6 and 7 are objected to because of the following informalities: Claim 6 is objected to since genus names should be italicized. Claim 7 is objected to since abbreviations should be spelled out upon their first recitation. Accordingly, Applicants has adopted the Examiner's suggestion and have amended claims 6 and 7. Applicants respectfully submit that this rejection has been overcome.

## **III. Claim Rejections 35 U.S.C. § 112**

Claims 1, 4-6, 8, 10-12 and 14-19 are rejected to under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. The Examiner states that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

The Examiner states that if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling. (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. Thus, Applicant assumes a certain burden in establishing that inventions involving physiological activity are enabled.

The Examiner states that the instant specification fails to provide significant direction on which bacteria, other than those set forth in Table 1, are capable of eliciting a modulated immune response when administered to an animal.

Applicant respectfully traverses the rejection. Applicant asserts that the application indeed enables the full scope of the claims. The arguments set forth in the Office Action suggest that not all bacteria subjected to the claimed method will result in eliciting an immune response in an animal when administered, it would require undue experimentation to identify bacteria that express SRFs.

Applicant respectfully disagrees with the Examiner's conclusions which are addressed in turn below. First, the Examiner states that to use the instant invention the skilled artisan must know which bacterial species are capable of producing SRFs in response to the cited stresses that are capable of modulating the immune system upon its administration to an animal. Office Action, at pages 4-5. The Examiner cannot be suggesting that Applicant is required to test all bacteria for it to be enabled- this simply is not the law. "The test [for enablement] is not merely quantitative, since a considerable amount of experimentation is possible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." (*In re Wands*, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988)). One skilled in the art would be able to make and use the present invention. Applicants' specification provides ample guidance to the skilled artisan seeking to produce a fraction of <10kDa that includes SRFs from bacteria.

Furthermore, there is no requirement that every possible bacteria produce SRFs when stressed and that the fraction of <10kDa having SRFs possess immunomodulatory activity. Enablement requires that one skilled in the art can identify operative embodiments without

engaging in undue experimentation. MPEP § 2164.06. The Federal Circuit has held that claims may encompass some inoperative species, so long as the number of inoperative species does not become significant and force one of ordinary skill in the art into undue experimentation in order to practice the invention. *Atlas Powder Co. v. E.I du Pont De Nemours & Co.*, 750F.2d 1569, 224 USPQ 409 (Fed. Cir. 1984). Therefore, once the initial discovery was made that the claimed method produces SRFs from stressed bacteria that are capable of modulating the immune system of an animal upon administration, there would be no difficulty in applying the claimed methods' recited steps to any other species or genera of bacteria, nor has the Examiner cited any arguments or evidence of such.

Second, the Examiner states that the specification is silent as to which "product" within the <10kDa fraction is responsible for some modulation and the efficacy of a given <10kDa fraction from a given stressed bacteria has to be determined empirically. Applicant respectfully reminds the Examiner that the claims are directed to methods of modulating the immune system of an animal - not the SRFs themselves and one skilled in the art would be able to follow the guidance in specification to obtain a fraction from stressed bacteria that is <10kDa that has SRFs.

Third, the Examiner admits that the specification is "enabling for methods for modulating the immune system of an animal ... wherein the bacteria is *Lactobacillus casei*, *Lactobacillus acidophilus*, *Lactobacillus fermentum*, *Lactobacillus plantarum*, *Listeria monocytogenes*, *Staphylococcus aureus*, *Salmonella typhimurium*, *Pediococcus acidolactici*, *Bacillus coryneforme*, *Escherichia coli*, *Enterococcus faecium*, *Streptococcus pyogenes* or *Klebsiella pneumoniae*". Office Action, page 3. Importantly, the given thirteen species are diverse in scientific taxonomy, for example, representing at least two different phylums and classes, three different orders, five different families, and eight different genera of bacteria. See attached

reference - TAXONOMIC OUTLINE OF THE PROKARYOTES BERGEY'S MANUAL OF SYSTEMIC BACTERIOLOGY, (2nd Edition 2004), in particular pages 114, 118, 122, 181, 186, 190-92, 194-95, 197, 200 and 299 (cited on the IDS and submitted herewith). The phenetic classification of these thirteen species into categories such as colony morphology, cell shape and arrangement, cell wall structure (Gram staining), virulence as a pathogen to humans, ability to form spores, natural habitat, and requirement for oxygen is diverse as well. The named species include those that are rods (bacilli), spheres (cocci), stain Gram-negative, Gram-positive, virulent and non-virulent pathogens, spore-formers, non-spore formers, and those that are aerobic and anaerobic. See attached references showing diversity - in particular pages 412, 413, 476, 478, 496, and 501 from Prescott L. M., Harley J. P., Klein D.A. MICROBIOLOGY (McGraw-Hill Inc., 4th edition 1999) and pages 114, 118, 122, 181, 186, 190-92, 194-95, 197, 200 and 299 from TAXONOMIC OUTLINE OF THE PROKARYOTES BERGEY'S MANUAL OF SYSTEMIC BACTERIOLOGY, (2nd Edition 2004) (both references are cited on the IDS and submitted herewith for the Examiner's consideration).

Indeed, the specification provides thirteen representative bacterial species as working examples using the methods of the present invention to produce SRFs. Attention should be directed to Example 1, in particular Table 1, which provides that all thirteen bacterial species produced SRFs when stressed according to the invention. Example 6 demonstrates the effect of a fraction of less than <10kDa from a representative bacterial species (*L. casei*) that activates macrophages.

The Examiner has provided no evidence to teach or suggest that this immunomodulatory effect observed from one bacterial species would not be expected from other species as well. The Examiner has not shown there would be any reason to doubt that other bacteria would not

perform in the same way when stressed (produce SRFs) and immunomodulate the immune system of an animal when administered.

In light of the disclosure, the skilled microbiologist would be able to carry out the full scope of the claimed invention without undue experimentation. To the extent that the bacteria expressed SRFs modulate the immune response in an animal when administered, persons skilled in the art would be able to determine whether a fraction of <10kDa produced according to the method of the present invention modulates the immune response in an animal. Therefore, exposing a bacteria to stress to generate/release SRFs and administering a fraction of <10kDa having SRFs to an animal is well within the knowledge and abilities of one skilled in the art. Therefore, the practice of this invention does not constitute undue experimentation.

In light of the foregoing remarks, it cannot be reasonably maintained that undue experimentation would be required to practice the invention. Applicant submits that they have satisfied the enablement requirement. Therefore, Applicant respectfully submits that claims 1, 4-6, 8, 10-12 and 14-19 are in form for allowance and request that the rejection under 35 USC §112 be withdrawn and reconsidered.

#### **IV. Conclusion**

It is respectfully submitted that Applicant is timely responding to the Notice of Non-Compliant Amendment and that no fees are required for this response. However, please consider this a request for any fees or extension inadvertently omitted, and charge those additional fees to Deposit Account No. 26-0084.

Reconsideration and allowance is respectfully requested.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Heidi S. Nebel", written over the typed name.

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